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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/502,283	02/11/2000	Sun Ai Raillard	02-029510US	4948

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	23

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/502,283	RAILLARD ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

Office Copy

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,12-17,19,20,22-78 and 81-126* is/are pending in the application.

4a) Of the above claim(s) *27-71,81-104,111,122 and 124* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12-17,19,20,22-26,72-78,105-110,112-121,123,125 and 126* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. The Response filed July 16, 2003 (Paper No. 22) is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 1-26 and 72-80 were pending (i.e., claims 27-71 were withdrawn in Paper No. 18 as being drawn to non-elected inventions and/or species). Applicants cancelled claims 7-11, 18, 21, and 79-80 in Paper No. 20. Furthermore, Applicants amended claims 1-6, 12-17, 19, 22-23, 26, 72-74 and 76-77. In addition, Applicants added claims 81-126. Therefore, claims 1-6, 12-17, 19-20, 22-26, 72-78 and 81-126 are pending.

Election/Restriction

4. Claims 81-104, 111, 122, 124 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected inventions and/or species (e.g., see Paper No. 9; see also Paper No. 22).

5. Therefore, claims 1-6, 12-17, 19-20, 22-26, 72-78, 105-110, 112-121, 123 and 125-126 are examined in this action.

6. This application contains claims 27-71, 81-104, 111, 122 and 124 drawn to a nonelected invention(s) and/or species. This was addressed in the previous action and in this office action. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Withdrawn Objections/Rejections

7. All previous rejections and/or objections are withdrawn in view of Applicants amendments and/or comments.

New Rejections

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

8. Claims 1-2, 12-16, 17, 19-20, 22, 72-76, 78, 105, 110, 112-115, 120-121, 123 and 126 are rejected under 35 U.S.C. 102(e) as being anticipated by Aebersold et al (U.S. Pub. No. 2002/0076739).

For ***claims 1-2***, Aebersold et al (see entire document) discloses analytical reagents and mass spectrometry-based methods using these reagents for the rapid, and quantitative analysis of proteins or protein function in mixtures of proteins (see Aebersold et al, abstract), which anticipates claim 1. For example, Aebersold et al discloses using ESI-MS to screen for β-galactosidase deficiencies in patients that have a lysosomal storage disease e.g., GM_1-gangliosidosis and in patients that are unaffected (i.e., the cells from the various patients constitute a gene library) (see Aebersold et al, page 11, column 2, last paragraph). Furthermore, Aebersold et al discloses purifying samples using streptavidin-agarose beads (i.e., a non-column-separated technique) wherein the purified samples were injected into ESI-MS to detect the presence of one or more components of interest (i.e., β-galactosidase in this case). In addition, Aebersold et al discloses live cells as required by claim 2 (see Aebersold et al, page 11, column 2, last paragraph).

For ***claims 12, 75 and 123***, Aebersold et al discloses the use of organic solvents for purification (e.g., see page 5, column 1, last three paragraphs).

For ***claims 13 and 110***, Aebersold et al teaches cell lysates (e.g., see page 3, paragraph 2).

For ***claims 14-16***, Aebersold et al teaches, for example, β-galactosidase and also -β-galactosidase substrates (see Aebersold et al, page 11, column 2, last paragraph).

For ***claims 17 and 112***, Aebersold et al teaches attaching a library to streptavidin-agarose beads (see Aebersold et al, page 11, column 2, last paragraph).

For ***claims 19-20, 113-114***, Aebersold et al discloses the β-galactosidase enzyme with a streptavidin binding affinity tag e.g., conjugates 3 and 4 including biotin and streptavidin (see Aebersold et al, page 11, column 2, last paragraph).

For ***claims 22, 115***, Aebersold et al discloses quantifying enzyme products and reactants (see Aebersold et al, page 11, column 2, last paragraph; see also page 2, column 2, paragraph 4).

For ***claims 72-73, 120-121***, Aebersold et al discloses centrifugation (see Aebersold et al, page 7, column 1, paragraph 3; see also page 10, column 1, paragraph 3; see also page 10, column 2, last paragraph).

For ***claim 74***, Aebersold et al discloses ion-exchange (e.g., see Aebersold et al, page 15, column 2, last paragraph; see also page 17, column 2, first paragraph).

For ***claim 76***, Aebersold et al discloses solid-phase extraction (e.g., see Aebersold et al, page 19, column 2, last two paragraphs; see also page 20, column 1, paragraph 1; see also Aebersold et al, page 11, column 2, last paragraph).

For ***claims 78 and 126***, Aebersold et al discloses pooling multiple samples (e.g., see Aebersold et al, page 7, column 1, paragraph 2; see also page 7, column 2, paragraph 4).

For ***claim 105***, Aebersold et al discloses a gene library that encodes among other enzymes β-galactosidase and N-acetyl-R-D-glucosaminidase from cultured fibroblast obtained from patients with lysosomal storage diseases and also from healthy individuals

(see Aebersold et al, page 11, column 2, last paragraph). These samples were purified using a "capture" technique employing streptavidin-agarose beads. Finally, the purified samples were analyzed by ESI.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-2, 12-17, 19-20, 22-26, 72-76, 78, 105, 110, 112-121, 123 and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al (U.S. Pub. No. 2002/0076739) and Siuzdak et al (Siuzdak, G. Mass Spectrometry for Biotechnology. New York: Academic Press. 1992).

For ***claims 1-2, 12-16, 17, 19-20, 22, 72-76, 78, 105, 110, 112-115, 120-121, 123 and 126***, Aebersold et al teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates claims 1-2, 12-16, 17, 19-20, 22, 72-76, 78, 105, 110, 112-115, 120-121, 123, 126 and, consequently, also renders obvious claims 1-2, 12-16, 17, 19-20, 22, 72-76, 78, 105, 110, 112-115, 120-121, 123 and 126.

The prior art teaching of Aebersold et al differs from the claimed invention as follows:

For ***claims 23-26, 116-119***, the prior art teachings of Aebersold et al differ from the claimed invention be not explicitly reciting the use of "neutral loss" and "parent ion" techniques. Aebersold et al only described the general use of a triple quadrupole mass spectrometer and general methods like collision-induced dissociation (e.g., see Aebersold et al, page 19, Exemplary MS^N Techniques and Instrumentation Section).

However, Siuzdak et al teaches the following limitations that are deficient in Aebersold et al:

For ***claims 23-26, 116-119***, Siuzdak et al discloses "neutral loss" and "parent ion" techniques are routinely used on "triple quadrupole" mass spectrometers employing "collision induced dissociation" techniques (e.g., see page 100, last paragraph; see also page 120, paragraph 3; see also figure 6.1).

It would have been obvious to one skilled in the art at the time the invention was made to use the method as taught by Aebersold et al with the "textbook" techniques as taught by Siuzdak et al because Siuzdak et al provides the basic background and practical

applications of mass spectroscopy including ESI specifically for biotechnology, which would encompass the screening method of Aebersold (i.e., the references represent analogous art). Furthermore, one of ordinary skill in the art would have been motivated to combine Siuzdak with Aebersold et al because Siuzdak et al teaches that structural information can be obtained for a broad range of systems including enzyme catalysis (e.g., see pages 122-126) and shows in detail how Aebersold et al could be modified to improve the enzyme catalysis and expand the capabilities of the method to other research areas.

12. Claims 1-6, 12-17, 19-20, 22-26, 72-78, 105-110, 112-121, 123 and 125-126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al and Siuzdak et al (U.S. Pub. No. 2002/0076739) and Siuzdak et al (Siuzdak, G. Mass Spectrometry for Biotechnology. New York: Academic Press. 1992) and Weinberg et al (WO 98/15969).

For ***claims 1-2, 12-17, 19-20, 22-26, 72-76, 78, 105, 110, 112-121, 123 and 126***, the combined teachings of Aebersold et al and Siuzdak et al teach all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 1-2, 12-17, 19-20, 22-26, 72-76, 78, 105, 110, 112-121, 123 and 126.

The combined prior art teaching of Aebersold et al and Siuzdak et al differs from the claimed invention as follows:

For ***claims 2-6, 77, 106-109 and 125***, the combined prior art teachings of Aebersold et al and Siuzdak et al differ from the claimed invention by not specifically

reciting the use of a "100 samples" in "less than an hour". Aebersold et al teaches that their screening method may be readily automated for high throughput, but does not discuss a rate (see Aebersold et al, page 12, column 2, paragraph 1).

However, Weinberg et al teaches the following limitations that are deficient in Aebersold et al and Siuzdak et al:

For ***claim 2-6, 77, 106-109 and 125***, Weiberg et al (see entire document) teaches that the "automated" mass spectrometer can reach speed "faster than 10, 1000, or 1000 library elements per second" (see Weiberg et al, page 6, line 28), which would read on 100, 200, 500, 1000 samples in less than an hour.

It would have been obvious to one skilled in the art at the time the invention was represent analogous art i.e., they all encompass the use of electrospray ionization mass spectroscopy. Furthermore, one of ordinary skill in the art would have been motivated to use the "high throughput methods" as taught by Weiberg et al with the combined teachings of Aebersold et al and Siuzdak et al because more samples could be studies in less time (e.g., see Weiberg et al, page 6, line 28). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Aebersold et al and Siuzdak et al teaches that high throughput methods can be used (see Aebersold et al, page 12, column 2, paragraph 1), which would include the methods of Weiberg et al.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D. Epperson, Ph.D. whose telephone number is (703) 308-2423. The examiner can normally be reached on Monday-Thursday from 9:30 to 7:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon D. Epperson, Ph.D.
September 30, 2003

BENNETT CELSA
PRIMARY EXAMINER